

SUMMARY OF SAFETY AND EFFECTIVENESS DATA

VISUDYNE[®] (verteporfin for injection) and the applicant's Ceralas I Laser and the Ceralink Slit Lamp Adapter comprise a combination product as defined in 21 CFR 3.2(e). The primary mode of action for the combination has been determined to be that of a drug and the Center for Drug Evaluation and Research (CDER) has been given administrative jurisdiction over the combination. Accordingly, information pertaining to the clinical studies to support the approval of the light device system described in PMA P050021 is contained within the New Drug Application (NDA) No. 21-119.

I. GENERAL INFORMATION

Device Generic Name:	Diode Laser
Device Trade Name:	Ceralas I Laser and Ceralink Slit Lamp Adapter
Applicant's Name and Address:	QLT, Inc 887 Great Northern Way Vancouver, British Columbia Canada V5T 4T5
PMA Number:	P050021
Date of Panel Recommendation:	None
Date of Notice of Approval:	December 20, 2005

II. INDICATIONS FOR USE

The Ceralas I Laser and Ceralink Slit Lamp Adapter are intended to be a light source for the photoactivation of the light activated drug VISUDYNE (verteporfin for injection) in photodynamic therapy for the treatment of patients with predominantly classic subfoveal choroidal neovascularization (CNV) due to age-related macular degeneration, pathologic myopia, or presumed ocular histoplasmosis.

III. CONTRAINDICATIONS

There are no known contraindications for the Ceralas I Laser or the Ceralink Slit Lamp Adapter for this indication for use. Refer to the drug package insert for any specific contraindications for the use of the drug VISUDYNE for these indications for use.

IV. WARNINGS AND PRECAUTIONS

Warnings and precautions for use of the Ceralas I Laser and the Ceralink Slit Lamp Adapter can be found in the Laser Operator Manual while precautions and warnings associated with the actual VISUDYNE photodynamic therapy can be found in the drug labeling.

V. DEVICE DESCRIPTION

The Ceralas I Laser is a semiconductor diode laser that provides power output of up to 500 mW of light at 689 nm. Dosimetry limits, including fluence and intensity, may be selected by the operator and displayed on the control panel. Refer to the Ceralas I Laser Operator Manual for the specific directions for use for setting the treatment parameters and for the specific directions for use for assembly and connection of the Ceralas I laser with the appropriate slit lamp adapter.

The Ceralas I Laser is comprised of an Indium, Gallium, Arsenide, (InGaAs), diode (treatment laser) emitting 689 nm, a diode laser (aiming beam) emitting 635 nm, control electronics and software, power supply, regulatory compliance safety features (i.e. safety shutter, safety interlocks, key lock switch, etc.), and a self-contained forced air cooling system. Laser energy is delivered to the patient through a fiber optic delivery system mated to slit lamp instruments.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Age-related macular degeneration (AMD) causes severe, irreversible vision loss and is the leading cause of blindness in individuals older than 50 years in the Western World. Most patients have the non-neovascular or “dry” form, characterized by drusen and atrophic changes in the retinal pigment epithelium (RPE). Eighty to 90 percent of the severe vision loss due to AMD, however, is attributable to the neovascular or exudative form, also known as the “wet” form, which is characterized by choroidal neovascularization (CNV). In CNV, the newly-formed vessels are accompanied by proliferation of fibrous tissue that can destroy

photoreceptors within 3-24 months as the areas of leakage become increasingly fibrosed and scarred, causing photoreceptors to atrophy resulting in extensive central scotoma. Without treatment, most affected eyes will have poor central vision (<20/200) within 2 years.

Various experimental therapies have been tried for CNV secondary to AMD but have thus far failed to show promising results. These therapies include interferon alpha, tissue plasminogen activator, and thalidomide. External beam radiation therapy has also been explored, with conflicting results, and the best-designed study to date has shown no effect. Surgical removal of neovascular lesions is under evaluation in randomized clinical trials. Another potential treatment, still in preliminary stages, is retrovirus-mediated gene transfer.

The only accepted treatment for neovascular AMD is laser photocoagulation. Several studies have shown that thermal laser photocoagulation is effective in treating CNV which is situated >200 μm from the foveal center (extrafoveal CNV) or within 1 to 200 μm from the foveal center (juxtafoveal CNV). When the CNV has extended to involve the geometric center of the foveal avascular zone (subfoveal CNV), the benefit of laser photocoagulation becomes much less clear since the destruction of photoreceptors overlying the area of the central fovea resulted in immediate vision loss. No substantial treatment benefit was observed until an average follow-up of 18 months after treatment has been reached.

Laser photocoagulation is indicated only for well-demarcated extrafoveal and juxtafoveal CNV lesions as well as for small, well-demarcated CNV subfoveal lesions that include a component of classic CNV, which account for approximately 10-20% of the patients who present with this disease. Recurrences following standard laser treatment occur in approximately 50% of cases.

VII. MARKETING HISTORY

The Ceralas I Laser System has not been marketed in the United States or any foreign country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Please refer to the information in the VISUDYNE[®] NDA (NDA 21-119) for full and summarized reports on the safety and effectiveness of this combination product

Potential adverse effects of the Ceralas I Laser could be related to inappropriate laser power levels or improper use of the device. Such events should not occur if the

conditions and instructions for use are followed, as fully described in the VISUDYNE Package Insert and Ceralas I Operator Manual.

If the laser power should drop so that the light dose delivered to tissue was below that needed to activate VISUDYNE, the treatment would fail. Conversely, if the laser power should be greater than expected, so that an excess light dose was delivered to tissue, some areas of adjacent normal tissue that should have been spared treatment could be damaged with resulting loss of vision. The Ceralas I Laser System incorporates an internal control system which controls the output power level from varying from the requested power level. This greatly reduces the chance of improper dosimetry due to the laser.

IX. SUMMARY OF PRECLINICAL STUDIES

The Ceralas I Laser was not included in the clinical trials used to support the NDA approval of VISUDYNE. Non-clinical studies have been conducted by the sponsor demonstrating that the Ceralas I laser does meet the same optical output specifications as the approved laser used in the VISUDYNE clinical studies and the current commercial laser systems. Non-clinical testing included spot size uniformity and stability, output power, wavelength spectral purity and stability, and ability to generate the required spot sizes and treatment doses within the time frame specified in the VISUDYNE directions for use.

QLT has established specifications for lasers to be used with their drug VISUDYNE. These specifications are based on a series of tests which are specified in the company's Standard Operating Procedures which spelled out the company's specific success criteria. The individual tests that are specified include:

1. Laser spot size between 1.0-5.0 mm for the laser only and for 1.0 – 8.0 mm when combined with the appropriate sight lamp and/or contact lenses. This value shall not deviate more than $\pm 10\%$.
2. Treatment beam power output in terms of actual power and in terms of stability of power during period of exposure. This requirement is that the deviation will not be more than $\pm 20\%$.
3. Spectral output for treatment beam both in terms of power in specifications and stability during treatment exposure. The requirement for both of these tests is that both the power and stability be greater than 90% within the $689\pm 3\text{nm}$ range specified for these lasers.

4. Beam profile in terms of circularity, uniformity and stability during treatment exposure. Circularity and uniformity of the beam had to be greater than 0.870 with circularity and uniformity sigma less than 20%. Output power within the beam could not exceed a variation of 20% with all devices and energies testing well below this specification.
5. Accuracy of exposure time to insure that treatment is not over exposure. This test does not have a performance specification in terms of accuracy of time since the laser systems are designed to insure that the correct exposure of 50J/cm² at 600 mW/cm² is delivered to the treatment site. When the lasers were tested to demonstrate that this dose was being correctly delivered, the laser on time was recorded as being 83-84 seconds for all tests. The actual timer setting used for the lasers in these tests was 83 seconds.

The Ceralas laser successfully met all of the specification requirements as established by QLT. In terms of beam spot size, except for the 1 mm spot, the laser spot size is well within the 10% requirement. At 1 mm the Ceralas laser was exactly 10%, however, this spot size is not a real world treatment value since the directions for use of VISUDYNE requires that the treatment spot have a zone of overlap of 500 microns around the treatment spot thus in real world use, the safety zone alone is 1 mm.

X. SUMMARY OF CLINICAL STUDIES

The results of the clinical studies for verteporfin under the conditions of use described in the labeling are presented in the VISUDYNE[®] NDA (NDA 21-119). A summary of this data is contained in the labeling for VISUDYNE.

XI. CONCLUSIONS DRAWN FROM THE STUDIES

The in vitro laboratory studies provide valid scientific evidence that the Ceralas I Laser met the same optical specifications as the lasers used in the in vivo and in vitro non-clinical laboratory studies and the clinical investigation reported in NDA 21-119. When combined with the material presented in NDA 21-119, these studies provide valid scientific evidence and provide reasonable assurance that the Ceralas I Laser is safe and effective when used according to the labeling.

Please refer to the conclusions presented in the VISUDYNE[®] NDA (NDA 21-119) in regard to the safety and effectiveness of verteporfin under the conditions of use described in the labeling. The VISUDYNE Package Insert contains a summary of the clinical trials with the appropriate warnings, contraindications, and precautions.

XII. PANEL RECOMMENDATION

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the General, Restorative and Neurological Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel

XIII. CDRH DECISION

Based on the information provided in this application, a decision was reached that this application was approvable for the requested indication for use. FDA issued an approval order on December 20, 2005. The applicant's manufacturing facility was inspected and was found to be in compliance with the Quality System Regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Information on the use of the Ceralas I Laser and the Ceralink Slit Lamp Adapter can be found in the Ceralas I Laser Operator Manual. Instructions for use of these devices for the photoactivation of the drug VISUDYNE can be found in the drug Package Insert and in the Operator Manuals.